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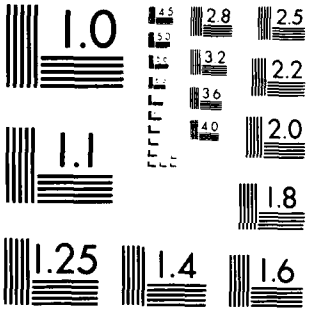

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Mechanisms of Retinal Damage from Chronic Laser Radiation

Annual Report

November 1976

Theodore Lawwill, M.D.,
S. Crockett, Ph.D.,
and
Glenna J. Currier, B.S.

1 September 1973
to
31 October 1976

Supported by

U. S. ARMY MEDICAL RESEARCH
AND
DEVELOPMENT COMMAND

Fort Detrick, Frederick, Maryland 21701-5012

Contract No. DAMD-17-74-C-4026

University of Louisville
Louisville, Kentucky 40202

Unclassified

SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

1a. REPORT SECURITY CLASSIFICATION Unclassified	1b. RESTRICTIVE MARKINGS
2a. SECURITY CLASSIFICATION AUTHORITY	3. DISTRIBUTION / AVAILABILITY OF REPORT Approved for public release; distribution unlimited
2b. DECLASSIFICATION / DOWNGRADING SCHEDULE	
4. PERFORMING ORGANIZATION REPORT NUMBER(S)	5. MONITORING ORGANIZATION REPORT NUMBER(S)
6a. NAME OF PERFORMING ORGANIZATION University of Louisville 6b. OFFICE SYMBOL (If applicable)	7a. NAME OF MONITORING ORGANIZATION
6c. ADDRESS (City, State, and ZIP Code) Louisville, Kentucky	7b. ADDRESS (City, State, and ZIP Code)
8a. NAME OF FUNDING / SPONSORING ORGANIZATION U.S. Army Medical Research & Development Command 8b. OFFICE SYMBOL (If applicable)	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER DAMD17-74-C-4026
8c. ADDRESS (City, State, and ZIP Code) Fort Detrick, Frederick, MD 21701-5012	10. SOURCE OF FUNDING NUMBERS

PROGRAM ELEMENT NO.	PROJECT NO.	TASK NO.	WORK UNIT ACCESSION NO.
62773A	3E162. 773A819	00	068

11. TITLE (Include Security Classification)
(U) Mechanisms of Retinal Damage from Chronic Laser Radiation

12. PERSONAL AUTHOR(S)
Theodore Lawwill, M.D. S. Corckett, Ph.D. and Glenna J. Currier, B.S.

13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (Year, Month, Day)	15. PAGE COUNT
Annual	FROM 9/1/73 TO 10/31/76	November 1976	

16. SUPPLEMENTARY NOTATION

17 COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
FIELD	GROUP	SUB-GROUP	
20	06		
20	05		

19 ABSTRACT (Continue on reverse if necessary and identify by block number)

20. DISTRIBUTION / AVAILABILITY OF ABSTRACT ☐ UNCLASSIFIED/UNLIMITED ☒ SAME AS RPT. ☐ DTIC USERS	21. ABSTRACT SECURITY CLASSIFICATION
22a. NAME OF RESPONSIBLE INDIVIDUAL Mrs. Virginia Miller	22b. TELEPHONE (Include Area Code) 301-663-7325
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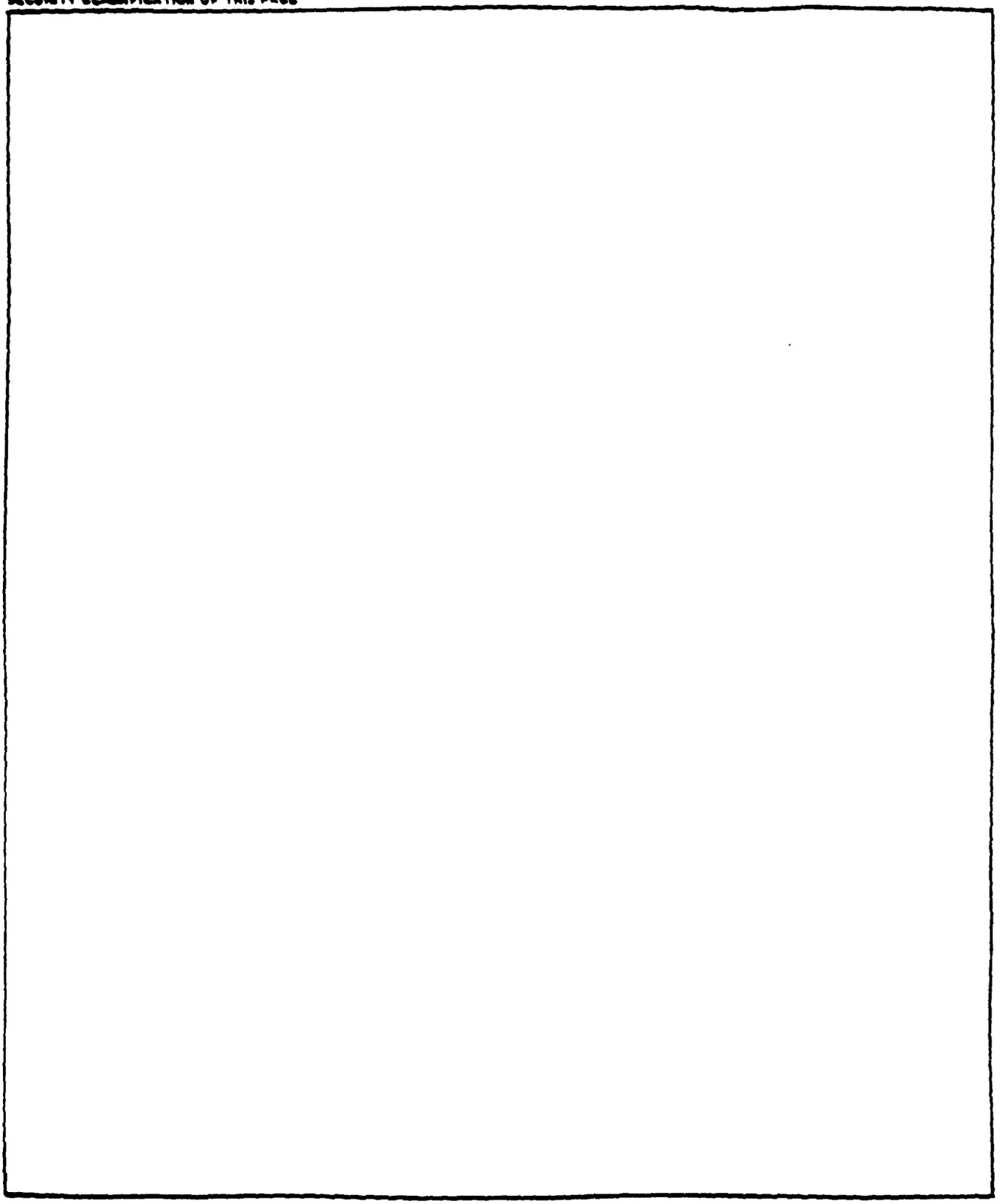

ABSTRACT

The effect upon the retina of exposure to large fields of bright visible light has been evaluated. The thresholds for retinal damage for four hour exposures in rhesus monkeys have been established for white light, argon laser lines of 514.5 nm, 488 nm, and 457.9 nm, and for 590 nm light from a dye laser. The damage has been evaluated by ophthalmoscopy, electroretinography, light and electron microscopy. The 457.9 nm light is more effective in causing damage, particularly histological damage, which is spread throughout the fundus and throughout the retinal layers. Functional damage shown by the electroretinogram follows a different spectral sensitivity curve without the increased effect in the blue. There appears to be more than one mechanism for retinal damage in chronic light exposure, and at least one mechanism is not dependent upon the visual pigment or the pigment epithelium. Thresholds appear to be within one or two log units of light levels encountered in normal visual experience.

Our work in light damage to the retina began in 1967, shortly after Noell's report[1] on retinal damage in rats. We have established the damage threshold for white light and several lines of the argon laser in rabbits[2] and monkeys[3,4,5]. The threshold for damage in these animals is at least three log units higher than that in the rat. Noell[6] has reported that in the rat the damage shows a spectral sensitivity similar to visual sensitivity. This spectral sensitivity is different from what we have found[4,5] and from that which Ham[7] has reported.

In our model, we are talking about exposing most of the posterior pole to an even illumination of moderately bright light for a period of hours. We are not talking about the thermal damage caused by small spot laser burns and photocoagulation. The level of light we use is unlikely to raise the temperature of the retina even one degree centigrade.

We are showing here not only that the threshold is lower with blue light, but that the morphological changes are different from

those previously described. Primary damage occurs in retinal layers which we think of as transparent to the damaging wavelength. We have found that no retinal layer has a threshold significantly different from other layers and that the variability throughout a single fundus is large.

In our appraisal, we evaluate damage induced by light by four measures: ERG, ophthalmoscopy, light and electron microscopy. Our methods of evaluation have been reported[4,8,9,10,11] and I will not present them again, except to say that histology is our most sensitive measure, closely followed by ERG. Ophthalmoscopy is the least sensitive and most variable measure.

The only change in our evaluation is that the histological change in each of six retinal layers is graded separately. Figure 1 is an electron micrograph showing the mildest effects of light on the pigment epithelium. There is a transformation of the pigment from the normal cigar-shaped bodies to rounder, larger, "balled-up" forms located more deeply in the cell. The earliest swelling of the mitochondria is shown.

This figure would be graded a plus or minus change of the pigment epithelium. Figure 2 shows 1+ changes of the pigment epithelium using light microscopy of a thick plastic embedded section. In this artificially folded retinal section, near the macula, there is some "balling-up" of the pigment epithelium. There are also early changes in the nuclei consisting of crenation. Figure 3 shows 3+ changes in the pigment epithelium with loss of pigment from pigment epithelial cells, swelling, and beginning formation of phagocytes. Pigment is included in the phagocytic cells rather than in the pigment epithelium in some cases. Figure 4 shows almost total loss of pigment epithelial cells with extensive phagocytosis in the area of the outer segments and pigment epithelium. This is a 4+ change as far as the pigment epithelium is concerned.

Figure 5 is an electron micrograph showing earliest distortions of the outer segments. This plus or minus change consists of vesicle

formations seen to the left of the photograph, and mild distortion of the outer segments. Figure 6 also shows plus or minus changes in the outer segment area. This swelling of outer segments is quite prominent as an early change, and may still be present up to two months after the initial insult. Figure 7 shows 2+ changes in the outer segments. There is severe distortion of the outer segment area and some of the outer segments are missing. Figure 8 shows 4+ changes with complete loss of the outer segments.

Figure 9 is an electron micrograph showing a swollen cone inner segment surrounded by normal rod inner segments. The mitochondria of the cone are particularly swollen, but the segment is most likely viable. This is graded as a plus or minus change of the inner segments. Figure 10 shows 1+ changes of the inner segments. The inner segments are more severely swollen, and there is a necrotic inner segment noted. Figure 11 shows 4+ changes with total necrosis of the inner segments.

Figure 12 shows 1+ changes in the outer nuclear layer. There is scattered pycnosis noted. Figure 13 shows 4+ changes in the outer nuclear layer, but only plus or minus changes in the inner nuclear layer.

There is extensive pycnosis in the outer nuclear layer while there is only swelling and occasional distortion of the nuclei in the inner nuclear layer. Figure 14 shows 1+ changes in the inner nuclear layer with more numerous pycnotic nuclei. Figure 15 shows extensive pycnosis in the inner nuclear layer, and is graded 2+ for this layer.

Figure 16 shows 2+ changes in the ganglion cell layer. The cells are swollen and a few are necrotic. Figure 17 shows 4+ changes in the ganglion cell layer with extensive changes and many pycnotic nuclei.

We have now exposed 87 monkey eyes to six different wavelengths of light at intensities between five microwatts and 100 milliwatts per square centimeter of retina. Our evaluation has included 3,000 ERG's, and histologic sections of 81 eyes. Two hundred thirty-one plastic embedded blocks on 26 eyes have been evaluated so far. We have recorded damage grades on each block for the six retinal layers, separately. These damage scores have been made into a histogram for each block each representing an area of the fundus. Reproductions of these histograms have then been placed on drawings which show the location in the fundus

from which the blocks were taken. The resulting pattern of damage has been evaluated subjectively. In Figure 18, block A1 includes the disc and block A3 includes the central macula. The lower line of the drawing represents the horizontal raphe. The central macula is spared, while the blocks on either side show more extensive changes. The area under the fiber layer next to the optic disc also shows less damage; as do the more peripheral areas.

The conclusions of this determination in 26 eyes are that:

(1) The damage is very patchy and varies randomly as to the retinal layer and fundus area most affected, except for specific changes in and around the macula and the optic disc.

(2) The central macular area consistently shows less damage than the area just surrounding the macula. The parafoveal and paramacular areas show the greatest amount of damage in all layers.

(3) As threshold is neared, the damage to the pigment epithelial and ganglion cell layers decreases most rapidly; and, at the lowest levels, the cone outer segments are the only structures affected.

(4) The retina underlying the thick nerve fiber layer around the nervehead is less affected than surrounding retina.

(5) In the macula, the thick internal layers may be affected when the pigment epithelium and outer layers show no changes.

The second area of interest is the relationship of functional change to histological change. As shown in Figure 19, the flash ERG returns to near normal after 2-4 weeks in spite of widespread severe ophthalmoscopically and histologically observed damage.

Figure 20 shows 4+ damage on a fundus photograph. There are widespread pigment epithelial defects noted. Figure 21 is an early fluorescein angiogram of the same fundus highlighting the pigment epithelial defects.

Histological sections are slightly more sensitive than ERG in detecting damage, but in the case of blue light there is an extreme discrepancy. Figures 22, 23 and 24 show the damage evaluation for all four techniques for all eyes in each exposure group, plotted

against exposure level. In Figure 22, our threshold data for white light shows 1+ damage at a little above five mw. In Figure 23, the data for the 5145 A. green line is not much different except that a greater chance of severe damage is present above threshold. In Figure 24, the threshold for the blue 4579 A. line is significantly different showing damage at one mw or less. There is no difference in damage between the several wavelengths as to which retinal layers sustain more damage. Figure 25 shows that the ERG damage score is only slightly less than the histology scores for the longer wavelength lines, but for the 4579 A. line (Figure 26) the histological damage is out of proportion to the functional ERG change.

The hypothesis that the receptors are primarily affected is not borne out by either the ERG or the histology.

In conclusion, in the range within one log unit of threshold, all cellular elements of the retina are susceptible to direct light damage. Therefore, it appears unlikely that the visual pigment or the visual

pigment cycle is uniquely related to the damage mechanism. Whatever the absorber is, it is more effective in the blue and is spread evenly throughout the retinal layers and throughout the fundus; except that the central macula appears protected while the peripheral macula, and just beyond, appears particularly susceptible. There is a discrepancy between the histologically observed damage and the functional damage shown by ERG. This discrepancy is significantly greater at shorter wavelengths. This might imply two mechanisms operating simultaneously -- one effecting histologically observable damage and one producing more transient functional changes.

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Figure 2

Figures 3 and 4

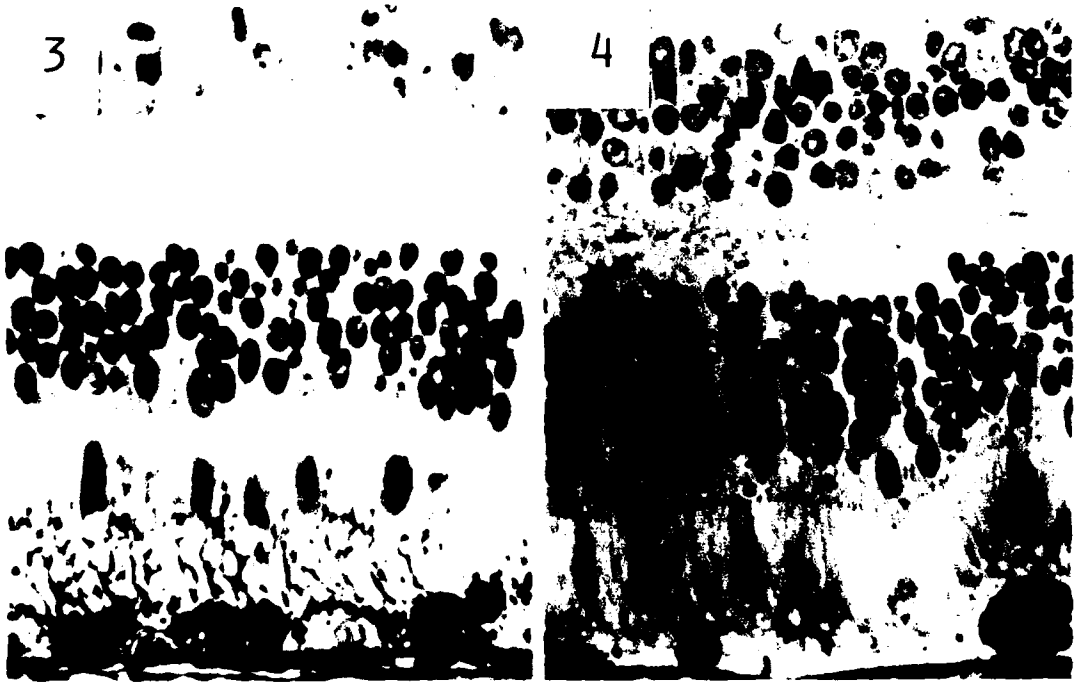
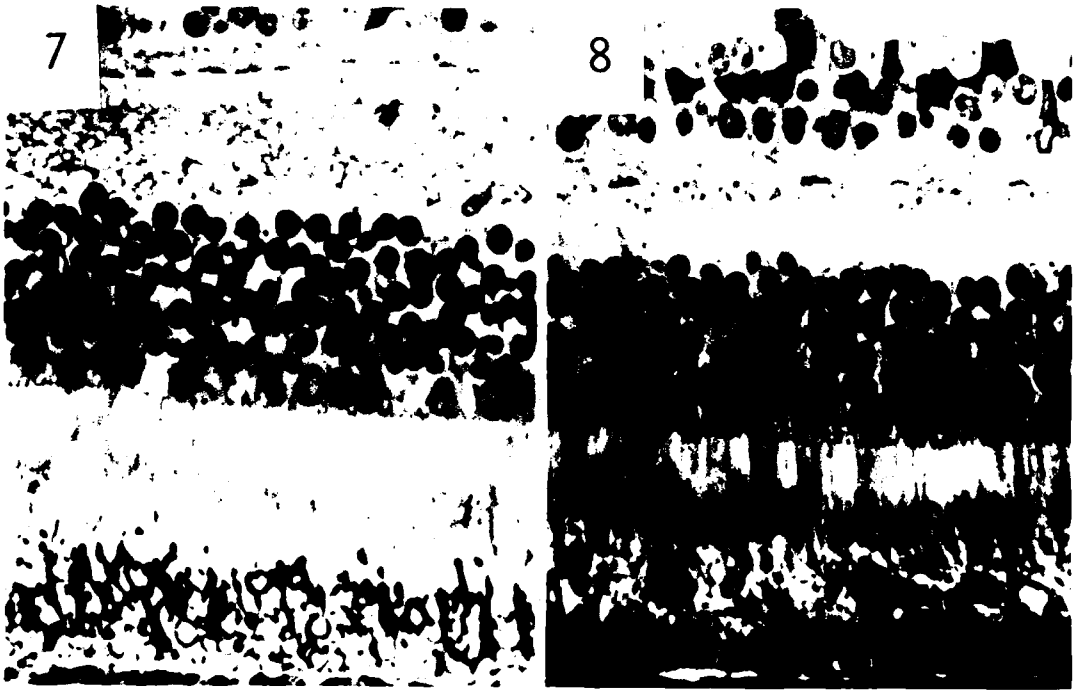


Figure 5

Figures 7 and 8



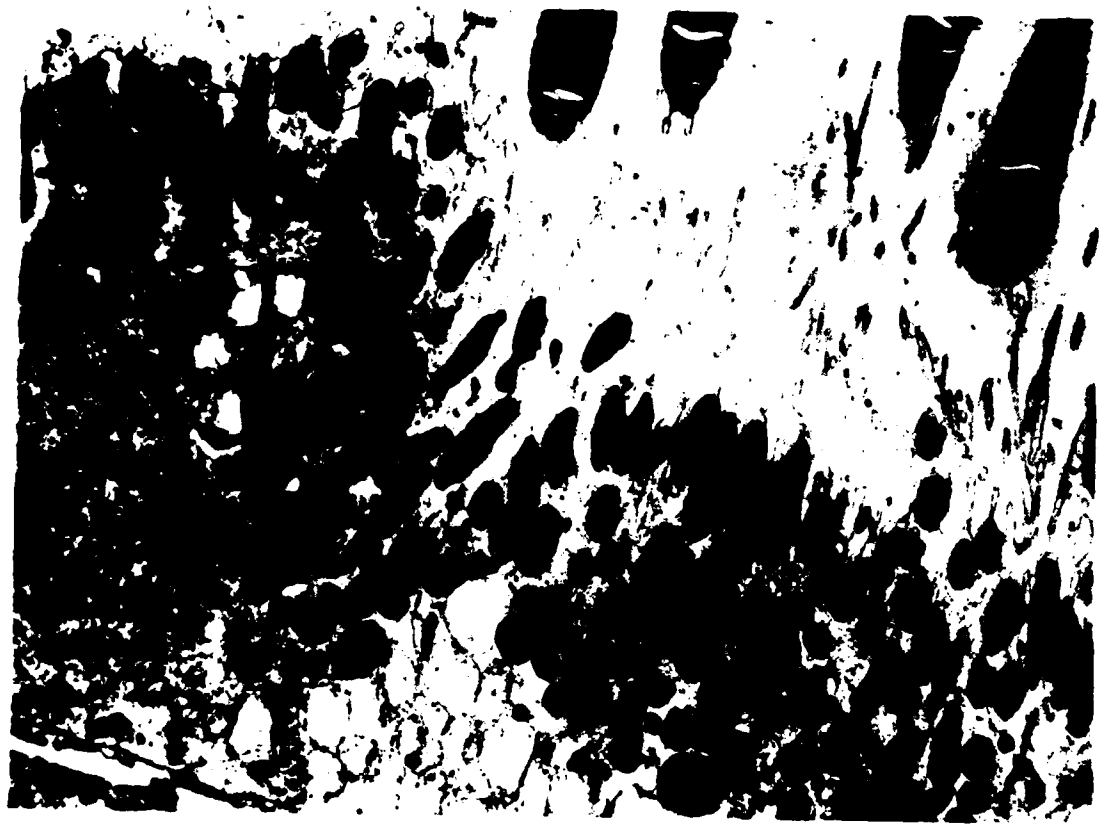


FIGURE 1

Figure 12

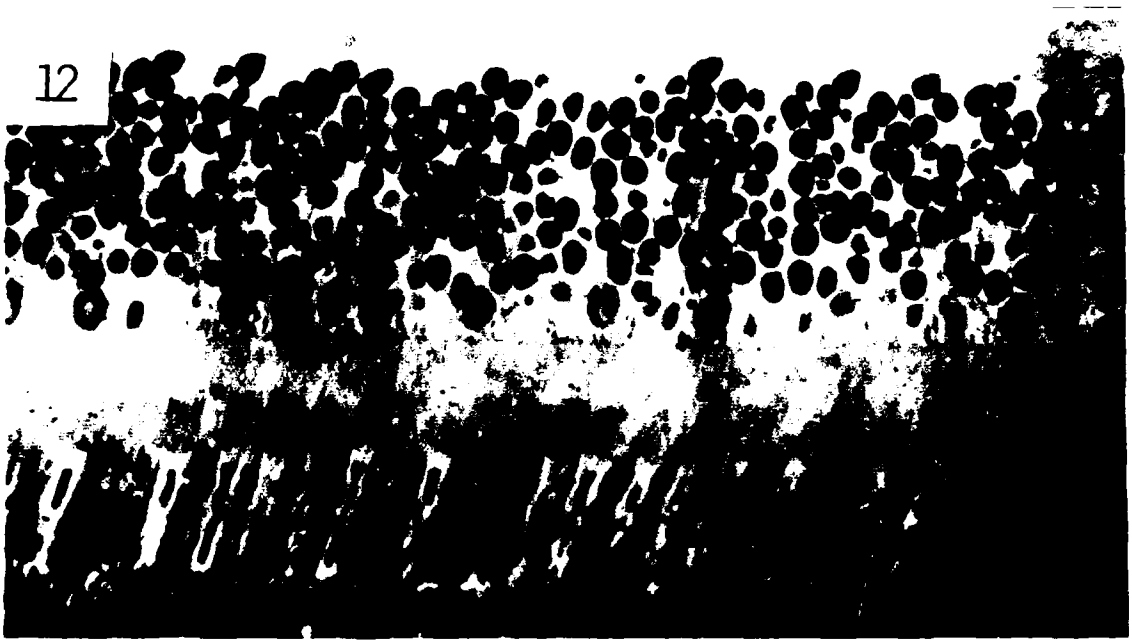


Figure 13

FIGURE 6

FIGURE 9

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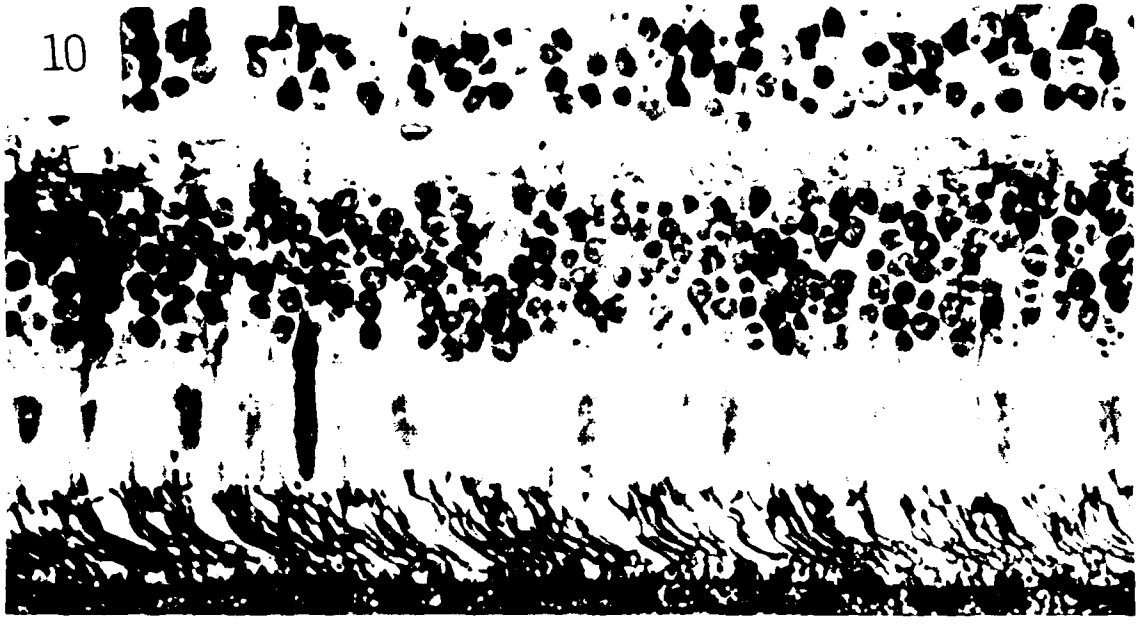

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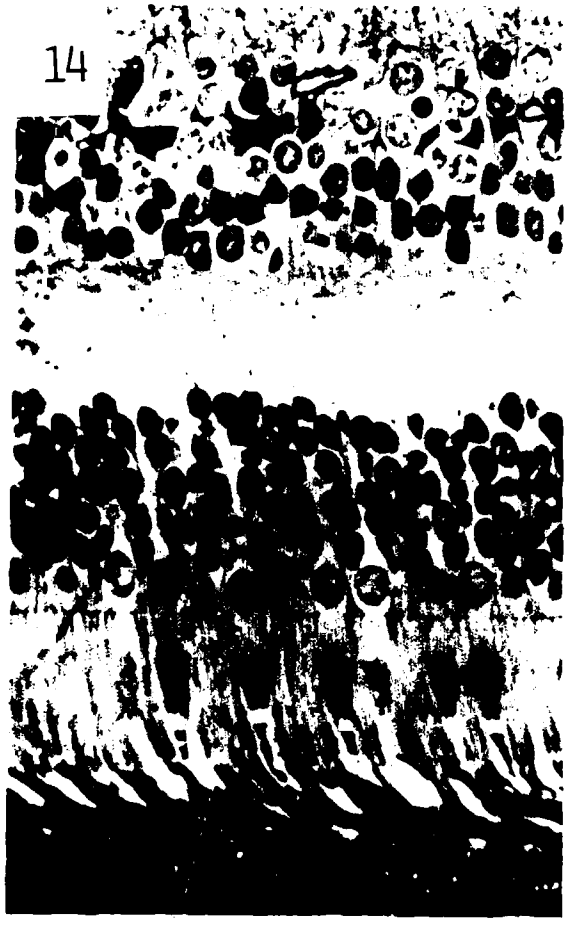
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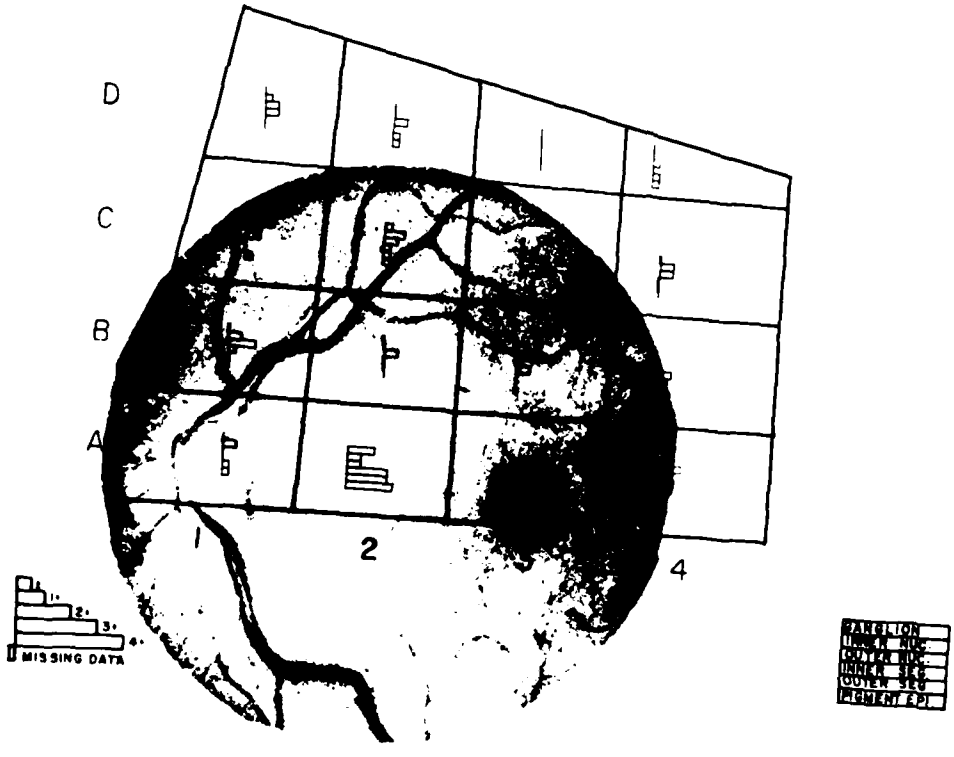
16

17



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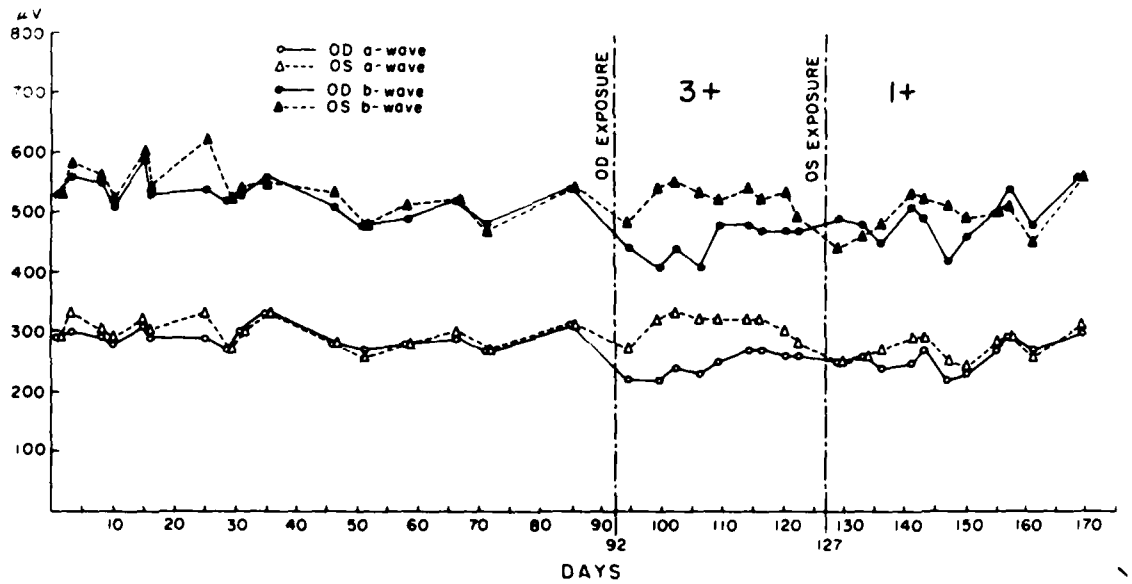
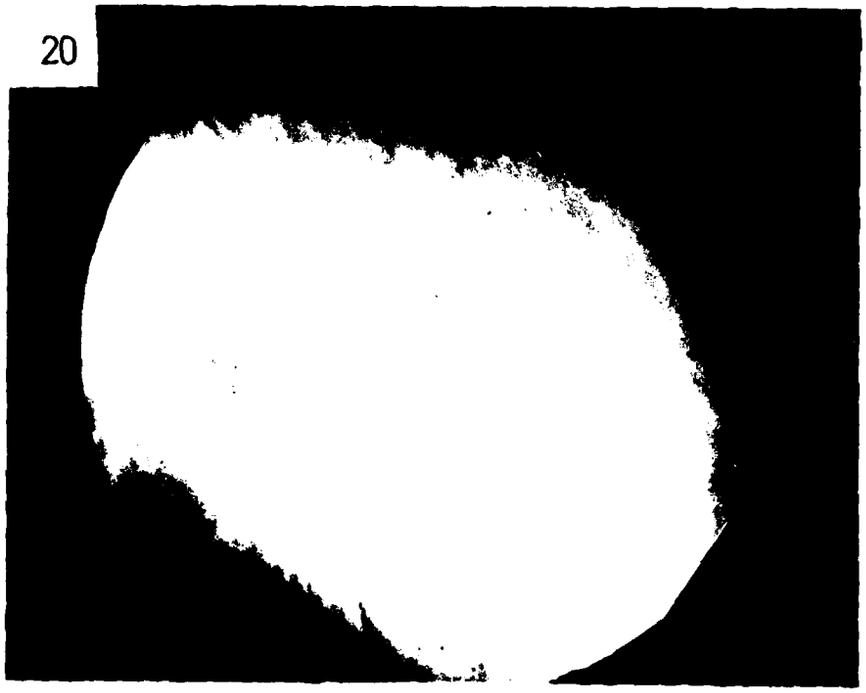

μV
800
700
600
500
400
300
200
100
OD a-wave
OS a-wave
OD b-wave
OS b-wave
OD EXPOSURE
OS EXPOSURE
3+
1+
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
92
127
DAYS

FIGURE 19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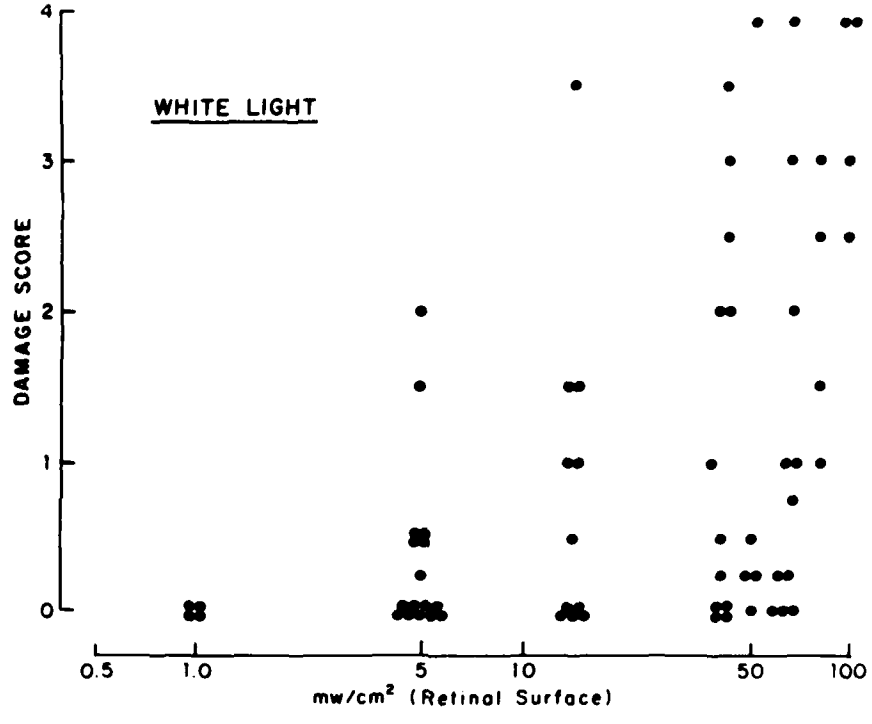

WHITE LIGHT
DAMAGE SCORE
0
1
2
3
4
0.5
1.0
5
10
50
100
mw/cm² (Retinal Surface)

FIGURE 22

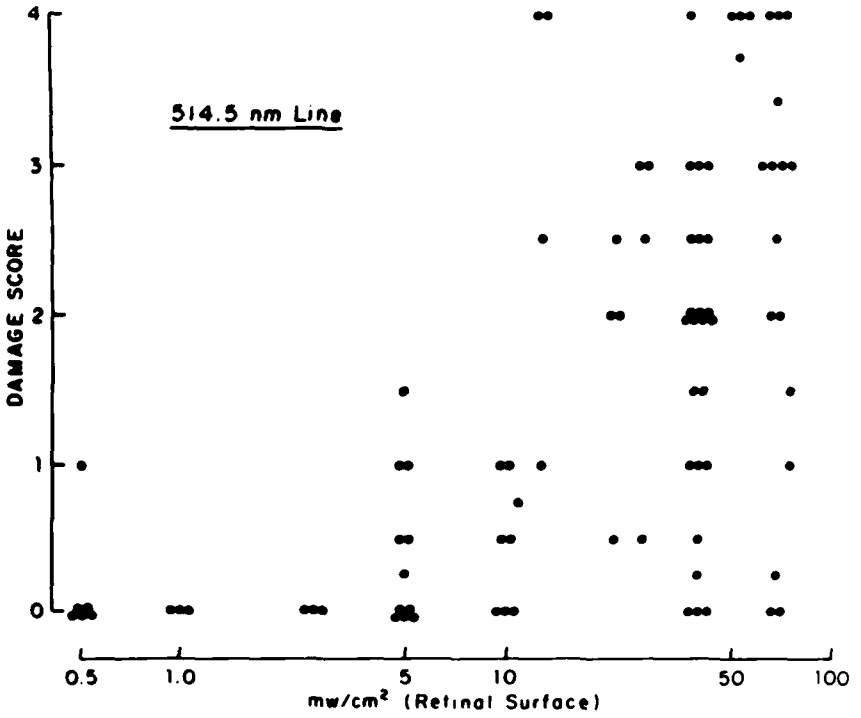

514.5 nm Line
DAMAGE SCORE
0
1
2
3
4
0.5
1.0
5
10
50
100
mw/cm² (Retinal Surface)

FIGURE 23

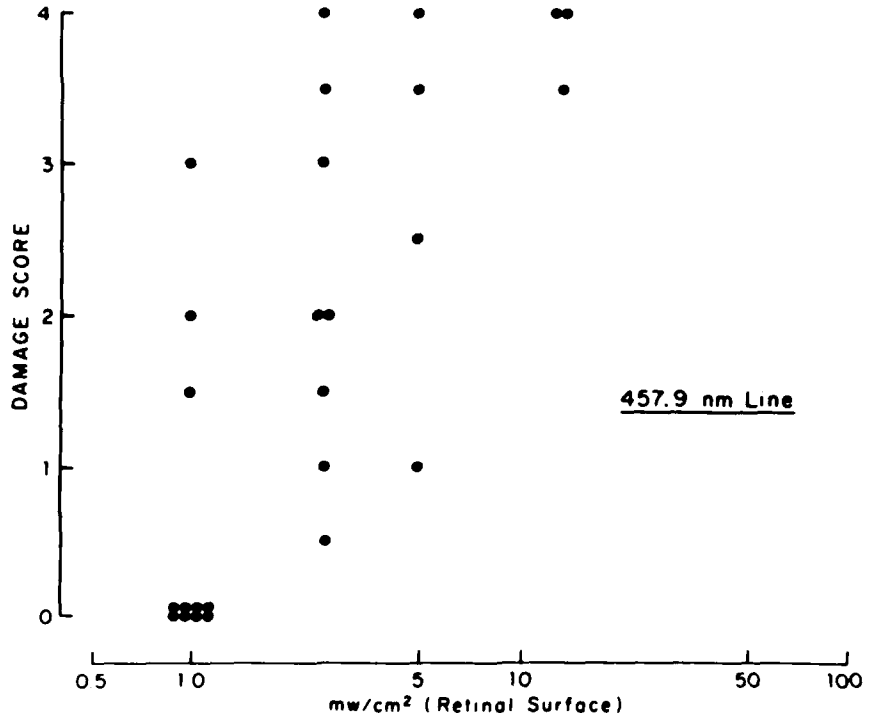

DAMAGE SCORE
4
3
2
1
0
457.9 nm Line
0 5
1 0
5
10
50
100
mw/cm² (Retinal Surface)

FIGURE 24

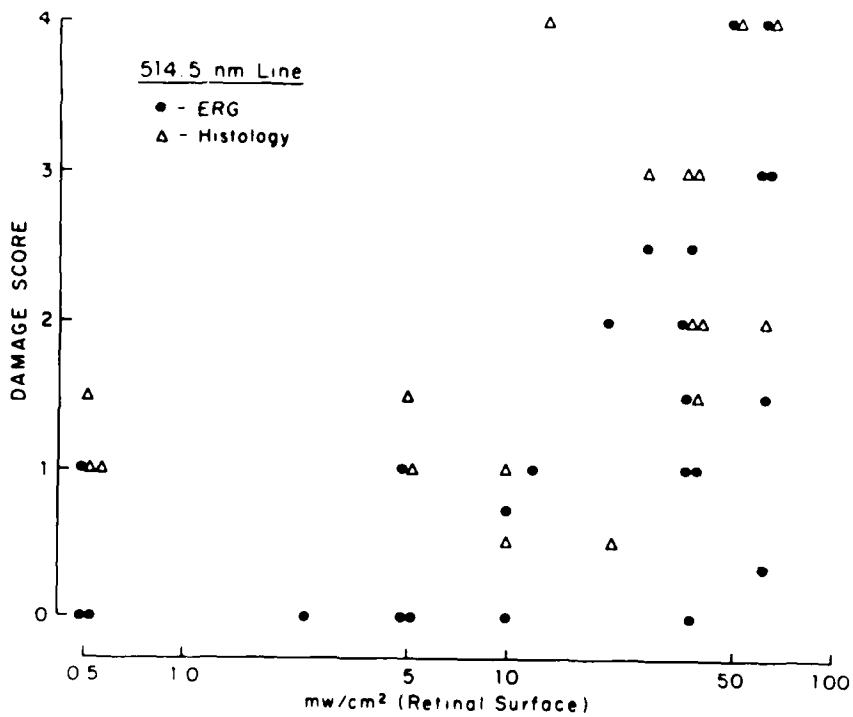
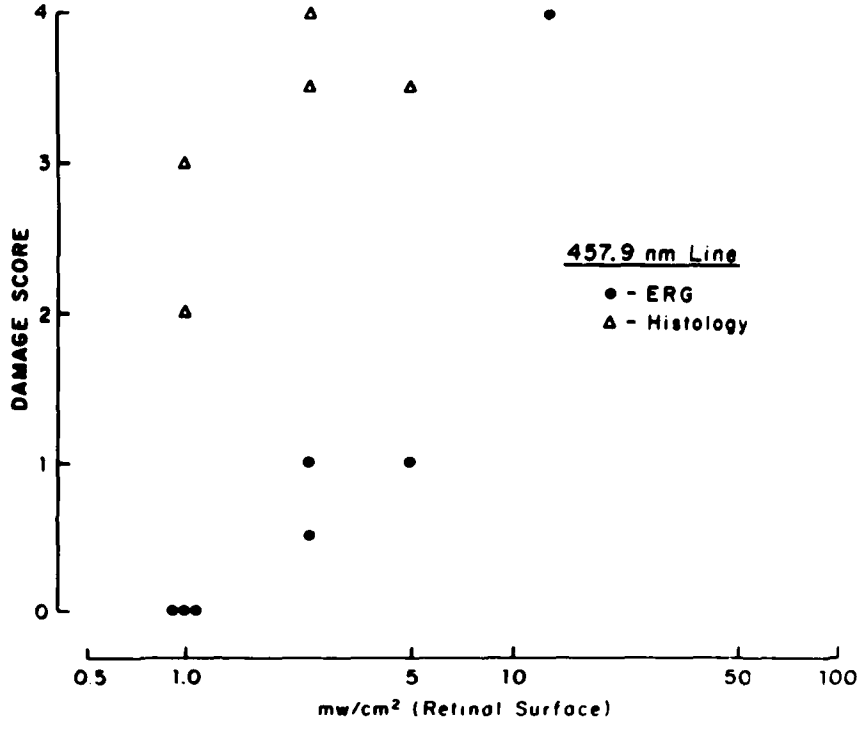

514.5 nm Line
● - ERG
Δ - Histology
DAMAGE SCORE
0
1
2
3
4
0.5
1.0
5
10
50
100
mw/cm² (Retinal Surface)

FIGURE 25


DAMAGE SCORE
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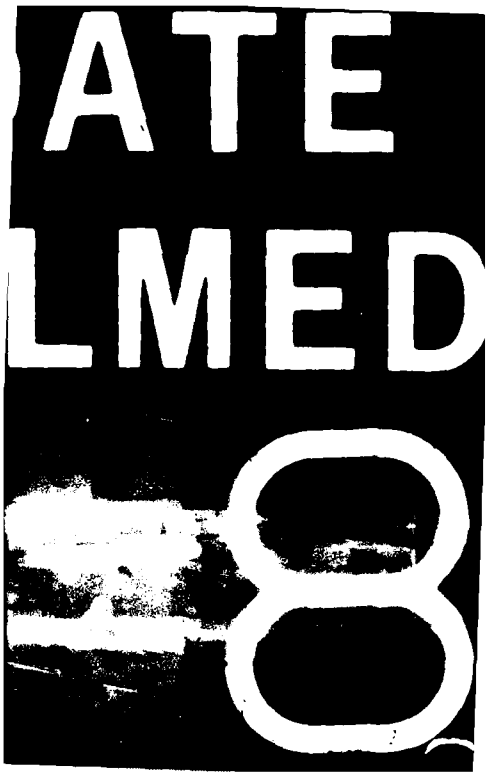
3
2
1
0
457.9 nm Line
● - ERG
Δ - Histology
0.5
1.0
5
10
50
100
mw/cm² (Retinal Surface)

FIGURE 26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